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BD1 CIP FWC IV

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Sherie L. Morrison et al.  
Serial No. : 08/266,154  
Filed : June 27, 1994  
For : METHODS FOR PRODUCING FUNCTIONAL  
IMMUNOGLOBULIN, INCLUDING CHIMERIC  
IMMUNOGLOBULIN, IN TRANSFORMED  
MAMMALIAN LYMPHOCYTIC CELLS  
Group Art Unit : 1806  
Examiner : Julie E. Reeves, Ph.D.

Hon. Assistant Commissioner  
for Patents  
Washington, D.C. 20231

May 18, 1998

**SECOND AMENDMENT AFTER ALLOWANCE**  
**PURSUANT TO 37 C.F.R. 1.312(a)**

Sir:

Applicants request approval under Rule 312(a) for entry of the following amendment without withdrawing the case from issue.

**IN THE TITLE**

Please replace the current title with:

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**METHODS AND TRANSFORMED MAMMALIAN LYMPHOCYTIC CELLS FOR  
PRODUCING FUNCTIONAL ANTIGEN-BINDING PROTEIN INCLUDING  
CHIMERIC IMMUNOGLOBULIN AND FRAGMENTS** ✓

**IN THE CLAIMS**

Please amend claims 129-131 and 134-137 as follows:

Q2

34 129. A method as recited in claim <sup>31</sup>126 wherein [each] the first chain comprises a constant region.

35 130. A method as recited in claim <sup>31</sup>126 wherein the heavy and light chain variable domains are from [domain is found in] a first mammalian species and the heavy and light chain constant domains are from [domain is found in] a second mammalian species, said second mammalian species being other than the first mammalian species.

Q3

34 131. A method as recited in claim <sup>34</sup>129 wherein the heavy and light chain variable domains are from [domain is found in] a first mammalian species and the heavy and light chain constant regions are from [region is found in] a second mammalian species, said second mammalian species being other than the first mammalian species.

Q4

39 134. A method as recited in claim <sup>37</sup>132 wherein prior to step (a) the cell endogenously produces an immunoglobulin light chain or an immunoglobulin heavy chain, [which endogenously-produced heavy chain is not secreted in a form capable of specifically binding to antigen,] but not both.

40 135. A method as recited in claim <sup>37</sup>132 wherein [each] the first chain [has] comprises a constant region.

Q5 14 136. A method as recited in claim <sup>39</sup>132 wherein the antigen-binding protein [immunoglobulin] comprises the heavy and light chain variable domains are from [domain found in] a first mammalian species and comprises the heavy and light chain constant domains are from [domain found in] a second mammalian species, said second mammalian species being other than the first mammalian species.

142 137. A method as recited in claim <sup>40</sup>135 wherein the antigen-binding protein [immunoglobulin] comprises the heavy and light chain variable domains are from [domain found in] a first mammalian species and comprises the heavy and light chain constant regions are from [region found in] a second mammalian species, said second mammalian species being other than the first mammalian species.

Please add the following claims 138-157.

Q6 143 138. A method for producing a functional antigen-binding protein comprising

- i) a first chain comprising an immunoglobulin heavy chain variable domain and an immunoglobulin heavy chain constant domain and
- ii) a second chain comprising an immunoglobulin light chain variable domain and an immunoglobulin light chain constant domain,

wherein the method comprises the steps of:

- (a) maintaining in a nutrient medium a transformed mammalian lymphocytic cell, said cell having been transfected with a first DNA molecule coding for the first chain of the protein and a second DNA molecule coding for the second chain of the protein;

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(b) expressing from said cell the first and second chains functionally assembled together to form said protein which is then secreted in a form capable of binding antigen; and

(c) recovering said antigen-binding protein,

wherein prior to being transfected, the cell does not express a functional immunoglobulin capable of specifically binding antigen.

~~139~~. A method as recited in claim ~~138~~ wherein prior to step (a) the cell does not endogenously produce any immunoglobulin chains.

140. A method as recited in claim 138 wherein prior to step (a) the cell endogenously produces an immunoglobulin light chain or an immunoglobulin heavy chain, but not both.

141. A method as recited in claim 138 wherein the first chain comprises a constant region.

142. A method as recited in claim 138 wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant domains are from a second mammalian species, said second mammalian species being other than the first mammalian species.

~~143~~ A method as recited in claim ~~141~~ wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant regions are from a second mammalian species, said second mammalian species being other than the first mammalian species.

~~144~~ A transformed mammalian lymphocytic cell producing a functional antigen-binding protein comprising

- Q6  
Cont.
- i) a first chain comprising an immunoglobulin heavy chain variable domain and an immunoglobulin heavy chain constant domain and
  - ii) a second chain comprising an immunoglobulin light chain variable domain and an immunoglobulin light chain constant domain,

wherein the transformed mammalian lymphocytic cell comprises:

(a) a first exogenous DNA molecule coding for the first chain of the protein; and

(b) a second exogenous DNA molecule, said second DNA molecule coding for the second chain of the protein;

wherein without the exogenous DNA molecules the cell does not express a functional antigen-binding protein.

50 145. A transformed mammalian lymphocytic cell as recited in claim 144<sup>49</sup> wherein without the exogenous DNA molecules the cell does not endogenously produce any immunoglobulin chains.

51 146. A transformed mammalian lymphocytic cell as recited in claim 144<sup>49</sup> wherein without the exogenous DNA molecules the cell endogenously produces an immunoglobulin light chain or an immunoglobulin heavy chain, but not both.

52 147. A transformed mammalian lymphocytic cell as recited in claim 144<sup>49</sup> wherein the first chain comprises a constant region.

53 148. A transformed mammalian lymphocytic cell as recited in claim 144<sup>49</sup> wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant domains are from a second mammalian species, said second mammalian species being other than the first mammalian species.

Q6  
cont.

~~54~~ <sup>52</sup> 149. A transformed mammalian lymphocytic cell as recited in claim ~~147~~

wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant regions are from a second mammalian species, said second mammalian species being other than the first mammalian species.

~~55~~ <sup>55</sup> 150. A transformed mammalian lymphocytic cell producing a functional antigen-binding protein comprising

i) a first chain comprising an immunoglobulin heavy chain variable domain and an immunoglobulin heavy chain constant domain and

ii) a second chain comprising an immunoglobulin light chain variable domain and an immunoglobulin light chain constant domain,

wherein the transformed mammalian lymphocytic cell comprises:

a plasmid comprising a first exogenous DNA molecule coding for the first chain of the protein and a second exogenous DNA molecule coding for the second chain of the protein; and

wherein without the exogenous DNA molecules the cell does not express a functional antigen-binding protein.

~~56~~ <sup>55</sup> 151. A transformed mammalian lymphocytic cell as recited in claim ~~150~~ wherein without the exogenous DNA molecules the cell does not endogenously produce any immunoglobulin chains.

~~57~~ <sup>55</sup> 152. A transformed mammalian lymphocytic cell as recited in claim ~~150~~ wherein without the exogenous DNA molecules the cell endogenously produces an immunoglobulin light chain or an immunoglobulin heavy chain, but not both.

Q6  
cont.

58 ~~155~~. A transformed mammalian lymphocytic cell as recited in claim ~~150~~ <sup>55</sup>

wherein the first chain comprises a constant region.

59 ~~154~~. A transformed mammalian lymphocytic cell as recited in claim ~~150~~ <sup>55</sup>

wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant domains are from a second mammalian species, said second mammalian species being other than the first mammalian species.

60 ~~155~~. A transformed mammalian lymphocytic cell as recited in claim ~~153~~ <sup>58</sup>

wherein the heavy and light chain variable domains are from a first mammalian species and the heavy and light chain constant regions are from a second mammalian species, said second mammalian species being other than the first mammalian species.

61 ~~156~~. A transformed mammalian lymphocytic cell produced by steps (a) and (b) of claim ~~126~~ <sup>31</sup>.

62 ~~157~~. A transformed mammalian lymphocytic cell produced by step (a) of claim ~~132~~ <sup>37</sup>.


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**REMARKS**

Applicants believe claims 138-157 are fully supported by the specification and respectfully request their entry and allowance.

Respectfully submitted,



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